

REMARKS

Status of the claims

Claims 1, 19, 28, 30, 31, and 33-50 were pending in the present application. By virtue of this response, claims 19, 28, 30-31, 33-38, and 42-44 have been canceled, claims 1, 39-41, and 45-50 have been amended, and new claims 51-55 have been added. Accordingly, claims 1, 39-41, and 45-55 are currently under consideration.

Support for the claim amendments and new claims may be found in the specification, for example, in Tables 2 and 3.

With respect to any claim amendments or cancellations, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Claim objection

Claim 33 is objected to as failing to further limit the subject matter of a previous claim. Claim 33 has been canceled herein, rendering this objection moot.

Rejections under 35 U.S.C. §112, second paragraph

Claims 33 and 40 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Claim 33 is rejected on the basis of the recitation of amino acids other than Val at position 194. Claim 33 has been canceled herein, rendering this rejection moot.

Claim 40 is rejected on the basis of the recitation of Ser at position 219. This language has been deleted from claim 40 as amended herein, rendering this rejection moot.

Claims 1, 19, 28, 30-31, and 33-50 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite with regard to recitation of “wild-type *Pseudomonas mendocina* cutinase” or “wild-type *P. mendocina* cutinase.” Although Applicants do not agree that “wild-type” is indefinite, for reasons of record, the claims have been amended herein to delete the term “wild-type” and to recite “SEQ ID NO:2” as the sequence of the *Pseudomonas mendocina* cutinase, rendering this rejection moot.

Rejections under 35 U.S.C. §112, first paragraph

Claims 30-31, 35, 37, and 40 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement with regard to double mutants at positions 192/194 and 192/219 of SEQ ID NO:2. Although Applicants do not agree that such embodiments are not supported by the specification, for reasons of record, the claims as amended herein do not recite these combinations of mutations, rendering this rejection moot.

Claims 1, 19, 31, 34-41, 44, and 46-50 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing new matter. Applicants respectfully traverse this rejection.

The Examiner contends that there is “a lack of support in the original application for a cutinase variant having a mutation at position 192 or 194 and any other mutations having the combination of increased polyesterase activity and enhanced thermostability.” The Examiner further contends that the term “containing” does not limit the claims to the specific substitutions recited therein. The claims have been amended herein to recite a variant of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2, wherein the amino acid sequence of the variant consists of specific recited substitutions disclosed in Tables 2 and 3 of the specification, and wherein the variant has an increased polyesterase activity and/or thermostability, as compared to the of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2. The “consisting of” language in the claims as amended clarifies that the claimed cutinase variants are limited to specific substitutions within SEQ ID NO:2.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 1, 19, 28, 30-31, and 33-50 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to disclose representative species to reflect the structural variation among the members of the genus. Applicants respectfully traverse this rejection.

The Examiner states that the claims have been construed as “encompassing a cutinase variant with a mutation at position 192 or 194 of SEQ ID NO:2 and any other mutations, wherein the variant has increased polyesterase activity and/or enhanced thermostability.” The Examiner further contends that “while the claims recite the specific mutation(s) corresponding to position(s) 192, 194, 192/194, or 192/194/219 of SEQ ID NO:2, the remaining sequence of the resulting variant polypeptide is completely undefined.”

As discussed above, the claims have been amended herein to recite a variant of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2, wherein the amino acid sequence of the variant consists of specific recited substitutions disclosed in Tables 2 and 3 of the specification, and wherein the variant has an increased polyesterase activity and/or thermostability, as compared to the of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2. The claims have been amended to clarify that the claimed cutinase variants are limited to specific substitutions within SEQ ID NO:2. The remaining sequences of the recited variants are thus defined in the claims as the sequence set forth in SEQ ID NO:2.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 1, 19, 28, 30-31, and 33-50 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled. Applicants respectfully traverse this rejection.

The Examiner states that “undue experimentation is required to make the full scope of the claimed cutinase variants.” The Examiner further states that the claims have been interpreted as “being drawn to a cutinase variant having mutation at position 192 and 194 *and any position(s) corresponding to SEQ ID NO:2*. As such, the claims broadly encompass a vast number of

cutinase variants without providing guidance regarding those variants that will likely exhibit the desired increased thermostability and optionally increased polyesterase activity.”

As discussed above, the claims have been amended herein to recite a variant of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2, wherein the amino acid sequence of the variant consists of specific recited substitutions disclosed in Tables 2 and 3 of the specification, and wherein the variant has an increased polyesterase activity and/or thermostability, as compared to the of the *Pseudomonas mendocina* cutinase consisting of the sequence set forth in SEQ ID NO:2. The claims have been amended to clarify that the claimed cutinase variants are limited to specific substitutions within SEQ ID NO:2. The claimed variants are enabled by virtue of their exemplification in the specification. Variants with the recited substitutions of SEQ ID NO:2 were tested and shown to have the recited properties of enhanced thermostability and/or increased polyesterase activity, as disclosed in the specification. It would not require undue experimentation for a skilled artisan to make and use the claimed variants.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §103(a)

Claims 1, 28, 39, 41-42, 47, and 49 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Poulouse et al., U.S. Patent No. 5,352,594 (“Poulouse”). Applicants respectfully traverse this rejection.

The Examiner states that “Poulouse et al. teach that it would be useful to modify *P. mendocina* cutinase in order to alter its perhydrolysis ratio, k_{cat} , and K_m (column 2, lines 52-54). In order to do this, Poulouse suggest altering an amino acid within ‘about six amino acids on either side of a catalytic amino acid’ of *P. mendocina* cutinase (column 5, lines 42-57).” The Examiner admits that “Poulouse et al. do not actually mutate an amino acid within ‘about six amino acids on either side of a catalytic amino acid’ of *P. mendocina* cutinase.” However, the Examiner contends that “it would have been obvious to one of ordinary skill in the art to mutate

position 178 or 180 of the *P. mendocina* lipase of Poulouse et al. (corresponding to amino acid 192 or 194 of SEQ ID NO:2 herein) with any amino acid.”

The claims as amended herein recite specific cutinase variants with specific substitutions of amino acids set forth in SEQ ID NO:2, as taught in the present specification to possess improved thermostability and/or polyesterase activities in comparison with the wild-type enzyme. Poulouse does not teach or suggest any of the presently claimed variants, as required to establish a *prima facie* case for obviousness.

Indeed, Poulouse states that with respect to substituting an amino acid within six residues of a catalytic amino acid, “[w]hile it is not possible to predict if the substitution will lead to an increase or decrease in the ratio [of perhydrolysis/hydrolysis], Applicant has discovered that either an increase or decrease will occur.” Col. 5, lines 63-66. Thus, the teachings of Poulouse do not provide a person of skill in the art with a reasonable expectation of success, as also required for a *prima facie* case for obviousness. *Poulouse clearly states that substitution of an amino acid within six residues of a catalytic amino acid does not provide predictable success with regard to alteration of perhydrolysis/hydrolysis ratio, and is completely silent regarding structural alterations that would provide increased polyesterase activity and/or enhanced thermostability, as currently claimed.*

Poulouse is not enabling with respect to the presently claimed variants. Merely suggesting that substituting an amino acid within six residues of a catalytic amino acid may result in an improvement in certain kinetic factors does not enable the specific variants exemplified in the present specification and currently claimed. A large number of potential variants are encompassed within the genus of polypeptides having a substitution within six residues of one of the three catalytic amino acids -- $6 \times 2 \times 3 \times 19 = 684$ possible variants for a single substitution. The claimed variants also encompass double and triple substitutions, which is an even larger genus. The large number of variants in the genus, coupled with Poulouse’s statement that it is not possible to predict how a particular substitution will affect kinetic parameters and the lack of teaching or suggestion that such substitutions would lead to increased polyesterase activity and/or thermostability for the *P. mendocina* cutinase enzyme, fail to provide

a skilled artisan with an expectation of predictable success in arriving at the claimed variants.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

Claims 30-31, 35, 37, 43-46, 48, and 50 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Poulouse. Applicants respectfully traverse this rejection.

The Examiner states that “Poulouse et al. further teaches that multiple substitutions within the six amino acids of the catalytic triad ‘can be done to optimize the results’” and that “[t]herefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to mutate position 178 or 180 and position 205 of the *P. mendocina* lipase . . . with any amino acid.” The Examiner admits, however, that “Poulouse et al. do not actually make a double mutant of *P. mendocina* cutinase as encompassed by the claims.”

Applicants submit that a suggestion that something “can be done” does not provide a reasonable expectation of predictable success, as required for an obviousness rejection. Poulouse does not teach any of the claimed variants, including those with multiple substitutions. As discussed above, the genus of variants with substitutions within six amino acids of multiple catalytic amino acids is very large, and Poulouse teaches that it is not possible to predict if even one substitution will lead to an increase or decrease in a substrate specificity ratio (col. 5, lines 63-66). *If it is not possible to predict the effects of substitution of one amino acid, it follows that substitution of two residues is even less predictable.* Further, Poulouse does not teach or suggest amino acid substitutions to alter the particular properties of *P. mendocina* cutinase that are currently claimed.

Thus, Poulouse does not teach or suggest all of the claim limitations (*i.e.*, specifically claimed variants) and does not provide a reasonable expectation of success in arriving at the claimed invention. Accordingly, the disclosure of Poulouse does not satisfy the elements for a *prima facie* case for obviousness.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

Claims 19, 33-34, 36, 38, and 40 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Poulouse. Applicants respectfully traverse this rejection. Applicants respectfully traverse this rejection.

The Examiner states that “Poulouse et al. further teaches that multiple substitutions within the six amino acids of the catalytic triad ‘can be done to optimize the results’” and that “[a]t the time of the invention, it would have been obvious to one of ordinary skill in the art to mutate position 178, 180, and position 205 of the *P. mendocina* lipase . . . with any amino acid.” The Examiner admits, however, that “Poulouse et al. do not actually make a triple mutant of *P. mendocina* cutinase as encompassed by the claims.”

As discussed above, a suggestion that something “can be done” does not provide a reasonable expectation of predictable success, as required for an obviousness rejection. Poulouse does not teach any of the claimed variants, including those with multiple substitutions. As discussed above, the genus of variants with substitutions within six amino acids of multiple catalytic amino acids is very large, and Poulouse teaches that it is not possible to predict if even one substitution will lead to an increase or decrease in a substrate specificity ratio (col. 5, lines 63-66). *If it is not possible to predict the effects of substitution of one amino acid, it follows that substitution of three residues is even less predictable.* Further, Poulouse does not teach or suggest amino acid substitutions to alter the particular properties of *P. mendocina* cutinase that are currently claimed.

Thus, Poulouse does not teach or suggest all of the claim limitations (*i.e.*, specifically claimed variants) and does not provide a reasonable expectation of success in arriving at the claimed invention. Accordingly, the disclosure of Poulouse does not satisfy the elements for a *prima facie* case for obviousness.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 07-1048, referencing Docket No. GC724. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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